

REMARKS

Applicants request reconsideration of the present application in view of the foregoing claim amendments and the remarks that follow.

Specification

The Office has requested amending the specification to correct a typographical error. Applicants provide an amended version of paragraph 34 to address this issue.

Status of the claims

Applicants have amended claim 8 to better describe the claimed method and cancel claim 15 without prejudice. Support for the amendment to claim 8 can be found throughout the specification, and, in particular, on page 3 and Example 1. Furthermore, claim 14 has been withdrawn from consideration as being drawn to a non-elected group. Claims 8-14 are under consideration.

Claim Rejections – 35 U.S.C. § 112 2nd paragraph/35 U.S.C. § 101

Claim 15 is rejected under 35 U.S.C. § 112 second paragraph, as being allegedly indefinite, and, under 35 U.S.C. § 101, for failing to fall within any of the defined statutory classes of patentable subject matter. Without acquiescing to the propriety of this rejection and in an attempt to further prosecution, Applicants have cancelled claim 15, thus rendering the §112-second paragraph and §101 rejections moot.

Non Obviousness of the Claims

Claims 8-13 and 15 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Avital (“Charcoal is a Sensitive, Specific, and stable Marker for the Diagnostic of Aspiration in Hamsters,” *Pediatric Research*, March 2002, pp. 397-401, Vol. 51, No. 3), in view of Joon (Assessment of Biodegradability of polymeric Microspheres in vivo: Poly(DL-lactic acid), and poly(L-lactic acid) and poly(DL-lactide-co-glycolide) microspheres, *Arch. Pharm. Res.* Vol. 16, No. 4, pp. 312-317, 1993). Applicants respectfully traverse.

Claim 15 has been cancelled, rendering the rejection of this claim moot.

The presently claimed invention is directed to a method for detecting pulmonary aspiration and gastroesophageal reflux (GER), by orally administering a diagnostic

composition of bio-degradable microspheres, and their detection within alveolar macrophages in a bronchoalveolar lavage. Neither Avital or Joon, both cited by the Office, teach or suggest the claimed methodology, or render the claimed invention obvious.

(i) Current Obviousness Standard

The U.S. Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a) and held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed and specifically stated:

Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason to combine the known elements in the fashion claimed*** by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex Inc., slip op. at 14 (emphasis added). As discussed below, the cited art cannot render the claimed invention obvious.

(ii) Avital in view of Joon

The Office's assertion that it would be obvious to substitute the charcoal particles used in Avital's diagnostic composition with Joon's polymeric microspheres is improper for at least the following reasons.

Avital discloses a method for diagnosing recurrent pneumonia in young children. Specifically, Avital discloses a diagnostic composition for detecting pulmonary aspiration by instillation of activated charcoal particles mixed with milk in the trachea of hamsters. Avital teaches that the use of charcoal as a diagnostic marker in young children suffering from recurrent pneumonia is limited, especially in light of hypercellularity observed in bronchoalveolar lavage (BAL), to 3 months after the instillation of charcoal particles. See Avital at page 400, right column. Nowhere does Avital teach or suggest a method that substitutes charcoal particles with bio-degradable microspheres, as claimed.

Joon, however, fails to remedy the defects in Avital. Although Joon discloses polymeric microspheres, the focus of this article is on assessing the factors that effect bio-degradability and the rate of bio-degradation of polymeric microspheres. To assess bio-degradation *in vivo*, Joon uses microspheres containing magnetite as a tracer and relies on the reticuloendothelial transport system to distribute and lodge the intravenously instilled polymeric microspheres in the liver and lungs of animals.

Importantly, Joon teaches homogenization of the lung tissue to isolate and recover the polymeric microspheres lodged within interstitial macrophages. Joon provides no guidance for obtaining BAL from the intravenously injected animals.

Joon, therefore, would not be understood by a skilled artisan to teach a method for detecting pulmonary aspiration or gastroesophageal reflux by detecting polymeric microspheres in alveolar macrophages, as claimed. Furthermore, even if Joon's teachings are combined with Avital, as suggested by the Office, the combination would fail to arrive at the inventive methodology that recites detecting "bio-degradable microspheres" within alveolar macrophages obtained *via bronchoalveolar lavage*. In fact, a skilled artisan, based on the teachings of Joon would conclude that the isolation of particles in Joon requires animal sacrifice, teaching away from the applicability of Joon as a diagnostic procedure. Therefore there would be no motivation to combine Joon with another reference that pertains to a diagnostic method for pulmonary aspiration.

Applicants submit that the examiner is using impermissible hindsight to support the case for *prima facie* obviousness. Joon provides no teachings for the use of its polymeric particles as markers for detecting pulmonary aspiration and GER and Avital is silent about

replacing charcoal as a marker in the disclosed diagnostic method with markers made of a bio-degradable polymer.

Claim 8 is not obvious over the combined teachings of Avital and Joon. Moreover, claims 9-13 depend from claim 8 and incorporate all its limitations. Thus, the dependent claims are also patentable for at least the same reasons mentioned above.

CONCLUSION

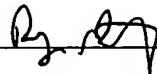
Having advanced credible grounds for obviating the obviousness issues, Applicants believe that the present application is now in condition for allowance and request the Office to provide an early indication to this effect. The Examiner is invited to contact the undersigned attorney if further issues remain that warrant discussion.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date October 5, 2009

By



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